

Mucosal vaccines are rising in popularity on a global scale due in part to: (1) the ease of administration of these vaccines as opposed to subcutaneous or other traditional means of administration; (2) the ease in facilitating self administration of mucosal vaccines as opposed to the traditional delays associated with assembling masses of people for traditional vaccine administration; and (3) the reduction and eventual elimination of hypodermic needles. An additional benefit of the development of effective mucosal vaccines is self administration, thus avoiding the necessity of trained personnel for traditional means of administration.

On page 5, line 9 replace the first paragraph with the following

Several substances with lipophilic or other characteristics which confer surfactant activity may increase absorption across mucosal membranes, thus increasing mucosal immunogenicity of vaccine antigens. Such excipients have been admixed to and tested as nasal adjuvants for diphtheria and tetanus toxoid, and compared with an aluminum-adsorbed vaccine given nasally in a human trial. A clear adjuvant effect was demonstrated, but local side effects were prominent, probably caused by the effect of the excipients on the epithelial membrane. The disruption of the membrane integrity also raises concerns regarding immune responses to other than the vaccine antigens concomitantly present at the mucosal surface.

On page 7, line 13 replace the first paragraph with the following:

HLT is a potent mucosal adjuvant, capable of inducing widely distributed, protective immune responses after intranasal delivery, and seems to be as effective as CT in inducing protective immunity. It is an effective adjuvant for serum and mucosal antibodies to more than one antigen administered simultaneously with HLT. Non-toxic mutants with preserved adjuvanticity have been constructed. However, it remains to be settled whether these mutants